Office Action Summary	Application No.	Applicant(s)	
	10/549,241	FERRARA ET AL.	
	Examiner	Art Unit	
	DANIEL C. GAMETT	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *72-122* is/are pending in the application.

4a) Of the above claim(s) *102-121* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *72-101 and 122* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 September 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *09/12/2005,11/30/2007*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This supplemental office action replaces the action mailed on 01/29/2008, which was incomplete due to omission of pages during preparation for mailing.

2. Applicant's election with traverse of claims 72-101 and 122 in the reply filed on 11/30/2007 is acknowledged. The traversal is on the ground(s) that the hematopoiesis stimulatory activity of Bv8, EG-VEGF, or a combination thereof, is a special technical feature of the claims that links Groups I and II so as to form a single inventive concept. This is not found persuasive because, while both Groups of invention generally address hematopoiesis, this biological phenomenon is not a technical feature of the claims. The claims define the invention. Claims 72-101 and 122 (Group I) are directed to methods comprising administration of Bv8, EG-VEGF, or a combination thereof, to achieve the effect of inducing proliferation of cells. Claims 102-121 (Group II) are drawn to methods comprising administering a Bv8 antagonist, EG-VEGF antagonist, or combination thereof, for the general purpose of treating an autoimmune disorder or a disorder associated with abnormal hematopoeisis; leukemias are recited as embodiments. Therefore, the two Groups are drawn to administration of completely different agents to achieve directly opposite results.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 102-121 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 11/30/2007.

4. Claims 72-101 and 122 are under consideration.

Information Disclosure Statement

5. The reference listed as Lin *et al.*, on the information disclosure statement filed 11/30/2007 has not been considered. It appears that no copy of this non-patent literature publication has been submitted in accordance with 37 CFR 1.98(a)(2).

Claim Objections

6. Claim 88 is objected to because of the following informalities: "lymophenia" is not in any dictionary and appears to be a misspelling of "lymphopenia". Appropriate correction is required.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claim 72-83, 85-99, 101 and 122 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The fact that a patent is directed to method entailing use of a compound, rather than to the compound *per se*, does not remove patentee's obligation to provide description of the compound sufficient to distinguish infringing methods from noninfringing methods (University of Rochester v. G.D. Searle & Co., 69 USPQ2d 1886 (CAFC 2004)). In this case, the claims are drawn to methods that comprise administration of genera of compounds recited as

Bv8, having at least 80% identity with an amino acid sequence of SEQ ID NO:2 or SEQ ID NO:4, or EG-VEGF, having at least having at least 80% identity with amino acids 20-105 of SEQ ID NO:8; each induces proliferation of endothelial cells.

9. To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, compound to be administered is recited only by name in the independent claims; the factors present in the dependent claims are a partial structure in the form of a recitation of percent identity and the functional limitation of inducing proliferation of endothelial cells. The expression "80% identity with *an* amino acid sequence of SEQ ID NO:X" could be met by any peptide in which 4 amino acids are identical to any 5 consecutive amino acids in the reference sequence. Thus, structurally, the genus is immense. Even if the claims recited 80% identity with *the* amino acid sequence of SEQ ID NO:X, this would result in greater than 3×10^{32} possible sequences for the 86 amino acid (20-105 inclusive) EG-VEGF polypeptide of claim 82, for example. The number of polypeptides 80% identical over the full lengths of SEQ ID NO:2 or SEQ ID NO:4 would be much larger, as these sequences are 129 and 108 amino acids in length, respectively. Although structural conservation among the related polypeptides is documented, the specification does not identify any particular portion of the structure that must be conserved in order to preserve the recited function. The instant specification describes only polypeptides consisting of SEQ ID NOs: 2, 4, 6, or amino acids 20-105 of SEQ ID NO: 8, as examples meeting the structural and functional limitations of the

instant claims. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

10. *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

11. With the exception of SEQ ID NOs: 2, 4,6, and 8, the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Possession may not be shown by merely describing how to obtain possession of members of the claimed genus or how to identify their common structural features. See *University of Rochester*, 358 F.3d at 927, 69 USPQ2d at 1895. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

12. Therefore, only isolated polypeptides comprising the amino acid sequences set forth in SEQ ID NOs: 2, 4,6, and 8, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear

that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

14. Claims 72-76, 82-90, 98-101, and 122 are rejected under 35 U.S.C. 102(e) as being anticipated by US 7264801, filed December 19, 2001, with a claim of priority from June 23, 2000 (of record).

The applied reference has a common assignee and one common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

15. US 7264801 discloses the same EG-VEGF which is the subject of the instant claims. US 7264801 discloses antibodies that specifically bind residues of 20-205 of EG-VEGF (see claims). The process of raising the claimed antibodies necessarily comprises contacting the progeny of bone marrow cells (e.g. antigen presenting cells) with EG-VEGF, and would cause proliferation

of B and T cells. The '801 patent teaches that EG-VEGF be administered as a purified protein or as a fusion protein and the EG-VEGF was administered to mice (column 63, lines 37-54; column 77, lines 42-46). These teachings anticipate the only positive steps recited in instant claims 72 and 86, and the forms of EG-VEGF recited in claims 72, 82-85, and 98-101. See *Bristol-Myers Squibb Co. v. Ben Venue Labs Inc.*, 246 F.3d 1368, 58 USPQ2d 1508 (Fed. Cir. 2001) (61 PTCJ 623, 4/27/01), where a patent for administering the anti-cancer drug paclitaxel was anticipated by a scientific article describing the same method but with no anti-tumor response. That court held that expressions of anti-tumor efficacy did not distinguish the claimed method from the prior art. The court further held that preamble language in claims of patents directed to administration of anticancer drug are expressions of purpose and intended result, and as such are non-limiting, since language does not result in manipulative difference in steps of claims. Therefore in the instant case, Applicant's assertions of an intended outcome and of a different result (inducing proliferation of bone marrow cells, lymphoid lineage cells, progenitor cells, or progeny thereof, or treating an immunodeficiency disorder, vs stimulating the production of antibodies) does not distinguish the claimed methods over the prior art. Likewise, the "wherein" expressions in claims 87-90 do not distinguish over the art because they simply expresses the intended result of a process step positively recited (MPEP 2111.04). Claim 122 is anticipated by the prior disclosure of EG-VEGF, which is necessarily held in a container as it is isolated, and non-functional printed material (instructions for use) do not distinguish a claimed product from the prior art (see MPEP 2112.01 [R-3] III).

16. Claims 72-81, 86-90, 93-97 and 122 are rejected under 35 U.S.C. 102(e) as being anticipated by US 6485938 (Sheppard), filed November 20, 2000, with a claim of priority to November 16, 1999. US 6485938 discloses Zven1, SEQ ID NO:2, which is identical to SEQ ID NO: 4 of the instant application, as shown by the following alignment:

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RESULT 1
US-09-712-529-2
; Sequence 2, Application US/09712529
; Patent No. 6485938
; GENERAL INFORMATION:
;  APPLICANT:  Sheppard, Paul O.
;  APPLICANT:  Bishop, Paul D.
;  APPLICANT:  Whitmore, Theodore E.
;  APPLICANT:  Thompson, Penny P.
;  TITLE OF INVENTION:  Human Zven Proteins
;  FILE REFERENCE:  99-81
;  CURRENT APPLICATION NUMBER: US/09/712,529
;  CURRENT FILING DATE:  2000-11-14
;  NUMBER OF SEQ ID NOS:  7
;  SOFTWARE:  FastSEQ for Windows Version 3.0
; SEQ ID NO 2
;   LENGTH: 108
;   TYPE: PRT
;   ORGANISM: Homo sapiens
US-09-712-529-2

  Query Match             100.0%;  Score 599;  DB 2;  Length 108;
  Best Local Similarity   100.0%;  Pred. No. 1.4e-54;
  Matches  108;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps
0;

Qy          1 MRSLCCAPLLLLLLLPPLLLTPRAGDAAVITGACDKDSQCGGGMCCAVSIWVKSIRICTP 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MRSLCCAPLLLLLLLPPLLLTPRAGDAAVITGACDKDSQCGGGMCCAVSIWVKSIRICTP 60

Qy         61 MGKLGDSCHPLTRKVPFFGRRMHHTCPCLPGLACLRTSFNRFICLAQK 108
              ||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 MGKLGDSCHPLTRKVPFFGRRMHHTCPCLPGLACLRTSFNRFICLAQK 108
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17. Sheppard teaches that Zven1 is expressed in eosinophils, peripheral blood lymphocytes and in B cell, T cell, monocyte, granulocyte, and myelocytic progenitor cell lines (column 3 lines 12-20; column 63, lines 20-40). Sheppard teaches administration of Zven1 (column 54, line 55-column 57, line 21) and fusion proteins comprising Zven1 (column 33, lines 1-33). These

teachings anticipate the only positive steps recited in instant claims 72-81 and 86-97. Applicant's assertions of an intended outcome does not distinguish the claimed methods over the prior art, since language does not result in manipulative difference in steps of claims. Claim 122 is anticipated by the prior disclosure of Zven1 (Bv8) polypeptide, which is necessarily held in a container as it is isolated, and non-functional printed material (instructions for use) do not distinguish a claimed product from the prior art (see MPEP 2112.01 [R-3] III).

18. Claims 72-76, 82, 84-90, 98-101, and 122 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent Application Publication 20030027998 (Holtzman), filed March 1, 2001. Holtzman discloses a polypeptide designated TANGO 266, SEQ ID NO:64. This disclosed polypeptide is identical to SEQ ID NO:8 of the instant application, as evidenced by the following excerpt from a search of the published patent application database with SEQ ID NO: 8 as the query sequence.

```
Title:          US-10-549-241-8
Perfect score:  589
Sequence:       1 MRGATRVSIMLLLVTVSDCA.........CSRFPDGRYRCSMDLKNINF 105

Scoring table:  BLOSUM62
                Gapop 10.0 , Gapext 0.5


                                     SUMMARIES

                 %
Result           Query
   No.   Score  Match Length DB  ID                          Description
 ----------------------------------------------------------------------------
     1     ------------------------------------------------------------------
    33     589  100.0    105  3  US-09-796-753-64            Sequence 64, Appl
```

19. Holtzman cultured bone marrow mononuclear cells and CD34+ human bone marrow cells in the presence of TANGO 266 expressed as an Fc-fusion protein [1005-1008, 1018] thereby anticipating the methods of instant claims 73-74, 82 and 84. Holtzman also transduced hematopoeitic progenitor cells with a vector to express TANO 266; the transduced cell were then transplanted into sublethally irradiated C57B16 mice and allowed to reconstitute the hematopietic system [1012-1013]. Thus, Holtzman treated an immunodeficiency disorder by administering TANGO 266 (EG-VEGF) as recited in instant claims 86-90 and 98-101. Holtzman further teaches administration of TANGO 266 for treatment of the full range of cells and conditions recited in instant claims 72-76 and 86-90 [1026-1032]. Claim 122 is anticipated by the prior disclosure of EG-VEGF, which is necessarily held in a container as it is isolated, and non-functional printed material (instructions for use) do not distinguish a claimed product from the prior art (see MPEP 2112.01 [R-3] III).

Conclusion

20. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DANIEL C. GAMETT, PhD., whose telephone number is (571)272-1853. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath N. Rao can be reached on 571 272 0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

DCG
Art Unit 1647
10 March 2008

/David S Romeo/
Primary Examiner, Art Unit 1647